

## REMARKS

Claims 29-40 and 70-77 are now pending. The Applicants respectfully request the Examiner to reconsider the rejections in view of amendments to the claims now presented and the following remarks.

### Claim Objections

The Applicants have addressed the objections to the claims as recommended. The Examiner is respectfully requested to withdraw all outstanding objections to the now pending claims.

### Rejections under 35 USC §112, paragraph 2

The Examiner has alleged that the subject matter of the claims is indefinite under 35 USC §112 ¶2.

The Applicants have amended the claims to address the issue raised by the Examiner. Particularly, the claims now specifically require that the subject is a mammal (specification, for example, at p.52, lines 1-5). The Applicants therefore respectfully request the Examiner to withdraw the rejections under 35 USC §112, paragraph 2.

### Introduction

The Applicants respectfully begin by pointing out that Dendritic Cells (DCs) are rare leukocytes that are uniquely potent in their ability to present antigens to T cells. The Applicants have specifically elucidated the mechanism wherein the infiltration and activation of dendritic cells is increased significantly upon exposure of the cells to compositions of the present invention unexpectedly resulting in an increased immune response.<sup>1</sup> Particularly, immunization is improved when nucleic acids are formulated with non-modified polyoxyethylene-polyoxypropylene block copolymers. Fewer polynucleotide molecules are required for an immune response, the time to raise the response is shortened, and there is no need for a booster injection. *Id, et seq.* In sharp contrast to the Examiner's stated position, enhanced ability of nucleic acids to cross cell membranes, *per se*, as taught by the art, does not result in the enhanced

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<sup>1</sup> Specification, for example, at p.9, lines 10-16.

activation of dendritic cells. Particularly, the prior art does not teach the activation of dendritic cells by means of administering nucleic acids formulated with non-modified polyoxyethylene-polyoxypropylene block copolymers. Principally, the methods of using non-cationic polyoxyethylene-polyoxypropylene block copolymer compositions of the present invention do not enhance the transport of polynucleotides across cell membranes as the Examiner suggests; yet, *unexpectedly* in view of the teachings in the art, activation of dendritic cells is induced. See, e.g., Specification at p.53, lines 22-24; Bioconj. Chemistry 13:937-944 (2002).<sup>2</sup>

### **Rejections under 35 USC §103**

A. The Examiner has alleged that the subject matter of claims 29, 31-32, 34, 36-37, 39-40, 69-70, 72 and 74-77 is obvious under 35 USC §103 over Raz, *et al.*, '940, in view of Kabanov, *et al.*, '611. Particularly, it is alleged that it would have been *prima facie* obvious to modify the methods taught by Raz, *et al.*, '940, by using the copolymer taught by Kabanov, *et al.*, '611, "because the copolymer could enhance the cell entry, thus the efficacy of the polynucleotide" (emphasis added). The Applicants respectfully point out that Kabanov, *et al.*, '611, particularly teach the therapeutic value and efficacy of polycationic copolymers to enhance cell entry of heterologous nucleic acids.

### **Raz, *et al.*, '940**

The '940 disclosure is drawn toward *specific immunostimulatory nucleic acids* and broadly contemplates a myriad of merely possible components of possible compositions of the active ingredient. As the Examiner has pointed out, Raz, *et al.*, indeed contemplate, *inter alia*, "co-polymers or block co-polymers"; however, the '940 disclosure does not contemplate, suggest, or describe polyoxyethylene-polyoxypropylene block co-polymers.

### **Kabanov, *et al.*, '611**

The '611 disclosure particularly teaches and stresses the advantages of polycationic polyether block copolymers compositions to increase the ability of nucleic acids to cross cell

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<sup>2</sup> Non-modified polyoxyethylene-polyoxypropylene block copolymers do not enhance DNA uptake, transgene expression, or DNase protection.

membranes; however, the '611 disclosure does not contemplate, suggest, or describe any method of inducing the activation of dendritic cells *or* any method of modulating an immune response.

The Applicants respectfully point out that the polyoxyethylene-polyoxypropylene block copolymers required to be within the subject matter of the claims now presented do not increase the ability of nucleic acids to cross cell membranes. See, e.g., Specification at p.53, lines 22-24. Yet, *unexpectedly*, the activation of dendritic cells is induced.<sup>3</sup> Since Kabanov, *et al.*, '611, specifically teach polycationic polyether block copolymers to enhance nucleic acid uptake, those of ordinary skill in the art would not be motivated to modify the Raz, *et al.*, '940 disclosure to employ non-modified polyoxyethylene-polyoxypropylene block copolymer to specifically activate dendritic cells. It is axiomatic that a claimed invention is not obvious solely because it is composed of elements that are all individually found in the prior art. See, e.g., *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457 (Fed. Cir. 1998).<sup>4</sup>

Accordingly, the Applicants respectfully request the Examiner to withdraw the rejection under 35 USC §103 of claims 29, 31-32, 34, 36-37, 39-40, 69-70, 72 and 74-77 now presented as obvious over Raz, *et al.*, '940, in view of Kabanov, *et al.*, '611.

**B.** The Examiner has further alleged that the subject matter of these same claims, i.e., 29, 31-32, 34, 36-37, 39-40, 69-70, 72 and 74-77 is obvious under 35 USC §103, this time over Carson, *et al.*, '877, again in view of Kabanov, *et al.*, '611.

The Applicants respectfully point out that the same fundamental legal weakness applies to the prospective combination of Carson and Kabanov and applies to the combination of Raz and Kabanov to reach the Applicants' now claimed invention, i.e., Kabanov in fact teaches away from compositions which employ non-modified polyoxyethylene-polyoxypropylene block copolymers. Both Carson *and* Kabanov stress and teach toward *cationic entities* to affect the efficacy of nucleic acid delivery.

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<sup>3</sup> Examples 60-61 (specification p.106-108) employ methods of the invention to exemplify the induction of dendritic cells thereby effecting the demonstrated infiltration and activation.

<sup>4</sup> The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984); MPEP §2143.01.

Accordingly, the Applicants respectfully request the Examiner to withdraw the rejection under 35 USC §103 of claims 29, 31-32, 34, 36-37, 39-40, 69-70, 72 and 74-77 now presented as obvious over Carson, *et al.*, '877, in view of Kabanov, *et al.*, '611.

C. The Examiner has further alleged that the subject matter of claims 30, 33, 35, 38, 71, and 73 is obvious under 35 USC§103 over Raz, *et al.*, '940, or Carson, *et al.*, '877 and Kabanov, *et al.*, '611, further in view of Kabanov, *et al.*, '438.

The Applicants respectfully point out that the same fundamental legal weakness again applies to the prospective combination of Carson, *et al.*, '877 or Kabanov, *et al.*, '611, and Kabanov, *et al.*, '438 to reach the Applicants' now claimed invention. Kabanov '611 in fact teaches away from compositions which employ non-modified polyoxyethylene-polyoxypropylene block copolymers. Both Carson and Kabanov '611 stress and teach toward *cationic entities* to affect the efficacy of nucleic acid delivery. Kabanov '438 formulations comprise metal and metal-chelating agents and are taught for the control of metal-dependant enzymes which play an important role in reproduction of pathogens. Kabanov '438 does not teach formulations for the administration of nucleic acids or for the activation of dendritic cells.

Accordingly, the Applicants respectfully request the Examiner to withdraw the rejection under 35 USC §103 of claims 30, 33, 35, 38, 71 and 73 as obvious over Raz, *et al.*, '940, or Carson, *et al.*, '877 and Kabanov, *et al.*, '611, further in view of Kabanov, *et al.*, '438.

### **Obviousness-Type Double Patenting Rejection**

The Examiner has rejected instant claims 29-40 and 69-77 as unpatentable over claims 2-3, 13, 18, 21 and 23 of Lemieux, *et al.*, '054.

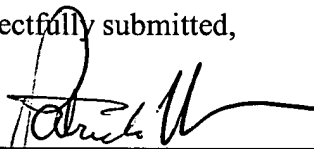
The Applicants respectfully elect to defer resolution of this issue at this time until the final scope of the now-pending claims to issue is determined. The Applicants indeed, however acknowledge their willingness to execute a terminal disclaimer under 37 CFR §1.321(c), if necessary.

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For all the foregoing reasons, the Applicants submit that claims 29-40 and 70-77 are in condition for allowance. Early action toward this end is courteously solicited. The Examiner is kindly encouraged to telephone the undersigned in order to expedite any detail of the prosecution.

A check in the amount of \$55.00 to cover the cost of the one-month extension is enclosed. The Commissioner is authorized to charge any deficiency or credit any overpayment in connection herewith to Deposit Account No. 13-2165.

Respectfully submitted,



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